

What is claimed is:

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- 5 1. A method for evaluating the ability of a compound to inhibit neurotoxicity which comprises:
- 10 (a) contacting a cell which expresses a receptor for advanced glycation end product protein and a mutant presenilin-2 protein in a cell culture and the compound;
- 15 (b) determining the level of cell death in the cell culture; and
- 20 (c) comparing the level of cell death determined in step (b) with the amount determined in the absence of the compound so as to evaluate the ability of the compound to inhibit neurotoxicity.
2. The method of claim 1, wherein the cell is a neuronal cell, a glial cell, a microglial cell, an astrocyte, an endothelial cell, a mononuclear cell, a tumor cell, or a PC12 cell.
- 25 3. The method of claim 1, wherein the compound is a peptide, a peptidomimetic, a nucleic acid, a polymer, or a small molecule.
4. The method of claim 1, wherein the compound is bound to a solid support.
- 30 5. The method of claim 1, wherein the mutant presenilin-2 is overexpressed.
- 35 6. A method for evaluating the ability of a compound to inhibit binding of an amyloid- β peptide to a receptor for advanced glycation end product which comprises:
- (a) contacting a cell which expresses a mutant

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presenilin-2 protein and a receptor for advanced glycation end product protein with amyloid- β protein and the compound;

- 5 (b) determining the amount of amyloid- β peptide bound to the cell;
- (c) comparing the amount of bound amyloid- β peptide determined in step (b) with the amount determined in the absence of the compound so as to evaluate the ability of the compound to inhibit binding of the amyloid- β peptide to the receptor for advanced glycation end product.
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7. The method of claim 1, wherein the cell is a neuronal cell, a glial cell, a microglial cell, an astrocyte, an endothelial cell, a mononuclear cell, a tumor cell, or a PC12 cell.

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8. The method of claim 1, wherein the compound is a peptide, a peptidomimetic, a nucleic acid, a polymer, or a small molecule.

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9. The method of claim 1, wherein the compound is bound to a solid support.

25 10. The method of claim 1, wherein the mutant presenilin-2 is overexpressed.

11. A pharmaceutical composition which comprises a compound capable of inhibiting neurotoxicity identified by the method of claim 1, and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11, wherein the carrier is a diluent, an aerosol, a topical carrier, an aqueous solution, a nonaqueous solution or a solid carrier.

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13. A method for treating a neurodegenerative condition in a subject which comprises administering to the subject an amount of the pharmaceutical composition of claim 11, effective to treat the neurodegenerative condition in the subject.
14. The method of claim 13, wherein the neurodegenerative condition is associated with Alzheimer's disease, diabetes, senility, renal failure, hyperlipidemic atherosclerosis, neuronal cytotoxicity, Down's syndrome, dementia associated with head trauma, amyotrophic lateral sclerosis, myasthenia gravis, multiple sclerosis or neuronal degeneration.
15. The method of claim 13, wherein the neurodegenerative condition is associated with degeneration of a neuronal cell in the subject.
16. The method of claim 13, wherein the neurodegenerative condition is associated with the formation of an amyloid- β peptide fibril.
17. The method of claim 13, wherein the neurodegenerative condition is associated with aggregation of amyloid- β peptide.
18. The method of claim 13, wherein the neurodegenerative condition is associated with infiltration of a microglial cell into a senile plaque.
19. The method of claim 13, wherein the neurodegenerative condition is associated with activation of a microglial cell by an amyloid- β peptide.
20. The method of claim 13, wherein the subject is a human.

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21. A transgenic non-human animal whose somatic and germ cells contain and overexpress a gene encoding human presenilin-2 protein and whose somatic and germ cells contain and overexpress a gene encoding human receptor for advanced glycation end product protein, the genes having been introduced into the animal or an ancestor of the animal at an embryonic stage and wherein the gene may be operably linked to an inducible promoter element.
22. The animal of claim 21, wherein the animal is a mouse.
23. The animal of claim 21, wherein the gene encoding human presenilin-2 protein is a mutant gene.
24. A method for identifying whether a compound is capable of ameliorating a neurodegenerative condition in an animal comprising:
- (a) administering the compound to the transgenic animal of claim 10, wherein the animal exhibits a neurodegenerative condition;
 - (b) measuring the level of neurodegeneration in the animal; and
 - (c) comparing the level of neurodegeneration measured in step (b) with the level of neurodegeneration measured in the animal in the absence of the compound so as to identify whether the compound is capable of ameliorating the neurodegenerative condition in the animal.
25. The method of claim 24, wherein the neurodegenerative condition is associated with Alzheimer's disease, diabetes, senility, renal failure, hyperlipidemic atherosclerosis, neuronal cytotoxicity, Down's syndrome, dementia associated with head trauma, amyotrophic lateral sclerosis, myasthenia gravis,

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multiple sclerosis or neuronal degeneration.

- 5 26. The method of claim 24, wherein the neurodegenerative condition is associated with degeneration of a neuronal cell in the subject.
- 10 27. The method of claim 24, wherein the neurodegenerative condition is associated with the formation of an amyloid- β peptide fibril.
28. The method of claim 24, wherein the neurodegenerative condition is associated with aggregation of amyloid- β peptide.
- 15 29. The method of claim 24, wherein the neurodegenerative condition is associated with infiltration of a microglial cell into a senile plaque.
- 20 30. The method of claim 24, wherein the neurodegenerative condition is associated with activation of a microglial cell by an amyloid- β peptide.
- 25 31. A cell comprising a recombinant nucleic acid which comprises DNA encoding mutant presenilin-2 protein and encoding receptor for advanced glycation end product protein.
- 30 32. The cell of claim 31 wherein the cell secretes mutant presenilin-2 and RAGE is transmembrane.
- 35 33. The cell of claim 31 wherein the cell is a neuronal cell, an endothelial cell, a glial cell, a microglial cell, an astrocyte, a smooth muscle cell, a somatic cell, a bone marrow cell, a liver cell, an intestinal cell, a germ cell, a myocyte, a mononuclear phagocyte, an endothelial cell, a tumor cell, a stem cell, or a PC12 cell.

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